

# Breast cancer in men: A 10-year experience of an oncology reference center in Northeast Mexico

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## ABSTRACT

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**Introduction:** Breast cancer in men (BCM) accounts for approximately 1% of all breast cancer cases. The present study aimed at describing the clinical and demographic characteristics of BCM in Mexican population. **Methods:** We performed a retrospective analysis of the men with newly diagnosed breast cancer treated in an oncology referral center in Northeast Mexico from 2007 to 2017. **Results:** Fifteen patients were included in the analysis. Mean age at diagnosis was 60.7 years and median time from diagnosis to the start of treatment was 2 months. About 73% of patients presented with locoregional disease (clinical stage [CS] I-III) and 26.7% were classified as Stage IV disease on their first assessment. All patients had invasive ductal carcinoma and 60.0% were Grade II tumors. Twelve cases were positive for hormone receptors and none showed overexpression of human epidermal growth factor receptor 2. Regarding primary treatment, 12 patients underwent a modified radical mastectomy and two underwent breast-conserving surgery. The majority of patients received chemotherapy and radiotherapy in the adjuvant setting and tamoxifen was the drug of choice in all patients considered as candidates for hormonal therapy. **Conclusion:** While most of the data presented matches that reported by other authors, some interesting differences unique to our population were observed.

**Key words:** Breast Cancer. Men. Mexico. Latin America.

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## RESUMEN

**Introducción:** El cáncer de mama en hombres (CMH) representa aproximadamente el 1% de todos los casos de cáncer de mama. El presente estudio tuvo como objetivo describir las características clínicas y demográficas del CMH en población mexicana. **Métodos:** Realizamos un análisis retrospectivo de los hombres con cáncer de mama recién diagnosticado tratados en un centro de referencia oncológica del noreste de México de 2007 a 2017. **Resultados:** Quince pacientes fueron incluidos en el análisis. La edad media al diagnóstico fue de 60,7 años, la mediana de tiempo desde el diagnóstico hasta el inicio del tratamiento fue de dos meses. El 73% de los pacientes presentaron enfermedad locorregional (EC I-III) y el 26.7% se clasificó como enfermedad en etapa clínica (EC) IV en su primera evaluación. Todos los pacientes tenían carcinoma ductal infiltrante y el 60% eran tumores de grado II. Doce casos fueron positivos para receptores hormonales y ninguno mostró sobreexpresión de HER2. Debido a limitaciones económicas, ninguno de los pacientes fue evaluado para determinación de mutaciones germinales o somáticas. Respecto al tratamiento primario, 12 pacientes se sometieron a mastectomía radical modificada y dos a cirugía conservadora. La mayoría de los pacientes recibieron quimioterapia y radioterapia en el escenario adyuvante y el tamoxifeno fue el fármaco de elección en todos los pacientes considerados candidatos a terapia hormonal. **Conclusión:** Si bien la mayoría de los datos presentados coinciden con lo reportado mundialmente por otros autores, se observaron algunas diferencias, tal vez únicas para nuestra población. (J CANCEROL. 2019;6:21-7)

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**Palabras clave:** Cáncer de mama. Hombre. México. América Latina.

## INTRODUCTION

Breast cancer in men (BCM) is an uncommon entity. It accounts for approximately 1% of all breast cancer cases, with a lifetime risk for men to develop breast cancer of 1:1000<sup>1</sup>. In the United States, SEER data estimate that 2550 men will be diagnosed with breast cancer in 2018, with 480 accountable deaths from this disease<sup>2</sup>.

There are important geographical variations regarding the incidence of this disease. A retrospective study compared the incidence of male breast cancer among several countries from five continents<sup>3</sup>. Israel reported the highest incidence with 1.24 cases per 100,000 men, while the Philippines and Japan reported the lowest rates with 0.16 and 0.18 cases, respectively. For countries in the European Union, the incidence rate ranged from 0.45

in Austria to 0.93 cases per 100,000 men in Iceland. In the United States, the incidence was 0.79 cases per 100,000 men. For Latin-American countries, incidence was lower than that reported by European countries or the United States. Among Latin-American countries, Colombia reported the lowest incidence with 0.23 cases, whereas Brazil reported the highest rates with 0.48 cases per 100,000 men. In Mexico, the reported incidence of male breast cancer in 2014 was 0.64 cases per 100,000 men<sup>4</sup>.

Large retrospective series of the clinical-pathological characteristics of female breast cancer in Mexican patients have been recently published<sup>5-7</sup>. However, there are limited data on this regard for male breast cancer<sup>8</sup>. The aim of this study is to describe the clinical and demographic characteristics of men with breast cancer treated at a referral center in Northeast Mexico within a 10-year period.

## METHODS

A retrospective, observational study was designed, in which medical records of male patients diagnosed with breast cancer attending for the 1<sup>st</sup> time to the breast tumor unit of the “Centro Universitario Contra el Cáncer – Hospital Universitario – UANL” in Monterrey, Mexico, were reviewed.

After the ethics committee approval, medical records of patients older than 18 years diagnosed with breast cancer from January 2007 to December 2017 were reviewed and included in the analysis.

The study variables included: age at initial diagnosis, body mass index, Eastern Cooperative Oncology Group performance scale (ECOG), comorbidities, risk factors, employment and marital status, primary tumor location, time from initial diagnosis to treatment, histologic type/grade, and initial clinical stage (CS) at diagnosis. Estrogen receptor (ER), progesterone receptor (PR), androgen receptor (AR), and human epidermal growth factor receptor 2 (HER2) status, as well as treatment received, were also included in the study.

For data analysis, SPSS v20 software was used. The normality of the variables was determined using the Shapiro–Wilk test. Variables with normal distribution were described using mean and standard deviation values. Variables with non-normal distribution were described with median and interquartile range (IQR) of percentiles 25 and 75. Categorical values were expressed in absolute numbers and percentages.

## RESULTS

A total of 15 cases of male breast cancer were obtained and included in the analysis, which corresponds to 0.5% of all cases of breast cancer diagnosed in our center. Mean age at diagnosis

**Table 1.** Patient characteristics

Patients	n = 15
Age at diagnosis (years); mean ± SD	60.7 ± 13.0
BMI (kg/m <sup>2</sup> ); median (IQR)	26.5 (25.0-30.4)
<b>Performance status; n (%)</b>	
ECOG 0-1	11 (73.3)
ECOG 2-3	4 (26.7)
<b>Risk factors; n (%)</b>	
Smoking	9 (60.0)
Alcohol consumption	11 (73.3)
Diabetes mellitus	6 (40.0)
SAH	8 (53.3)
Dyslipidemia	1 (6.7)
Hepatopathy	1 (6.7)
Family history	6 (40.0)

SD: standard deviation; IQR: interquartile range; BMI: body mass index; ECOG: Eastern Cooperative Oncology Group; SAH: systemic arterial hypertension; ICS: inherited cancer syndromes.

was 60.7 ± 13.0 years. Socioeconomic characteristics were as follows: eight patients reported to be employed at the time of their first evaluation and two had a higher education grade. Twelve patients (80.0%) had government-issued medical insurance.

About 73.3% of patients had an ECOG of 0-1, while 26.7% were classified as having a score of 2-3. Risk factors for BCM such as smoking, alcohol consumption, diabetes mellitus, and systemic arterial hypertension were present in 60.0, 73.3, 40.0, and 53.3% of patients, respectively. A total of six patients reported having a family history of cancer. None of the patients were evaluated for germline or somatic mutations. Epidemiological and clinical characteristics of patients are described in Table 1.

About 86.7% of patients presented with a retroareolar lump as their initial symptom. Median time from diagnosis to treatment was 2.0 months (IQR 1.75-7.5). Locoregional disease (CS I-III) at diagnosis was found in 73.3% of patients, while 26.7% of patients were considered to have Stage IV disease at initial presentation. Among patients with

Stage IV, three of them presented with recurrent systemic disease after having received primary treatment at another institution.

All patients had invasive ductal carcinoma (IDC) histology and were classified as having histological tumor Grades I, II, or III in 13.3, 60, and 26.7% of cases, respectively. Lymphovascular invasion was documented in 10 of 15 patients. Expression of ERs and/or PR was observed in 12 of 15 patients. None of the patients overexpressed HER2 by immunohistochemistry. Three patients were considered as triple negative and out of the two patients evaluated for expression of AR, two stained positive for this marker. Proliferation index as measured by Ki67 nuclear staining could only be obtained in one patient (Ki67 40%).

The majority (80.0%) of patients underwent modified radical mastectomy as their primary surgery and only two patients were amenable to breast-conserving surgery (BCS) with sentinel lymph node biopsy. The latter were considered as having CS II and neither presented with recurrent disease (RD) during follow-up. One patient was not offered primary surgery due to the presence of metastatic disease at initial diagnosis. The only patient who presented with CS I disease was not offered a breast-conserving approach. About 86.6% and 73.3% of patients received chemotherapy and radiotherapy in the adjuvant setting, respectively, while 60% of patients received hormonal therapy with tamoxifen. RD was observed in 26.7% of patients with only one patient showing recurrence after primary treatment at our institution. Among patients with RD, sites of recurrence were bone (two patients), lung (two patients), and brain (one patient). Disease characteristics are described in Table 2.

## DISCUSSION

The rarity of male breast cancer (0.5-1% of all cases) and thus the absence of established

**Table 2.** Disease characteristics

<b>Patients</b>	<b>n = 15</b>
Retroareolar primary tumor location; n (%)	13 (86.7)
TFDIT (months); median (IQR)	2 (1.0-7.0)
<b>Pathological characteristics, n (%)</b>	
Invasive ductal carcinoma	15 (100)
<b>Tumor grade, n (%)</b>	
I	2 (13.3)
II	9 (60.0)
III	4 (26.7)
<b>Immunohistochemistry, n (%)</b>	
Estrogen receptor positive	10 (66.7)
Progesterone receptor positive	10 (66.7)
HER2 positive	0 (0)
HR negative, HER2 negative	3 (20.0)
<b>Clinical stage, n (%)</b>	
I	2 (13.3)
II	7 (46.7)
III	2 (13.3)
IV	4 (26.7)
<b>Primary treatment, n (%)</b>	
Modified radical mastectomy	12 (80.0)
Breast conservative surgery + SLNB	2 (13.3)
No surgery	1 (6.7)
<b>Adjuvant treatment, n (%)</b>	
Chemotherapy	13 (86.6)
Radiotherapy	11 (73.3)
Hormonotherapy (tamoxifen)	9 (60.0)
<b>Recurrence after primary treatment, n (%)</b>	<b>4 (26.7)</b>

TFDIT: time from diagnosis to treatment; IQR: interquartile range; HR: hormone receptor; SLNB: sentinel lymph node biopsy; HER2: human epidermal growth factor receptor 2.

screening programs for this population cause significant delays in the diagnosis and treatment of this disease, which directly impacts the prognosis and survival of patients.

## EPIDEMIOLOGY

In our study, age at diagnosis of patients was considerably lower than described in other reports (68.4 years)<sup>4,9</sup>. Furthermore, studies have shown

that an increased time from diagnosis to treatment has been related to poor outcomes<sup>10</sup>. The median time from diagnosis to treatment in our study was 60 days, resembling data published by other authors.

CS at diagnosis is a known major prognostic factor for survival in both female and male patients with breast cancer, with 5-year survival rates of 75-100%, 50-80%, and 30-60% for patients with Stages I, II, and III, respectively<sup>11</sup>. The EORTC 10085/TBCRC/BIG/NABCG International Male Breast Cancer Program retrospectively analyzed the clinical characteristics and outcomes of 1822 cases of male breast cancer over a 20-year period. In this study, 94.9% of patients were diagnosed in early stages of the disease (56.2% pN0) and only 5.1% of patients were diagnosed with metastatic disease at initial diagnosis<sup>9</sup>. Contrastingly, in our population, most patients were found to have locally advanced or advanced disease at diagnosis, which could be in part explained by the lack of awareness of this disease on this particular population and poor access to health care.

## BRCA-1 AND 2 MUTATIONS

In retrospective series, a positive family history for breast or ovarian cancer has been found in 15-20% of cases, translating this into a risk ratio for breast cancer of 2.5<sup>9</sup>. In the study by Basham et al., only five of 94 men were carriers of the BRCA2 mutation with an accumulated risk of developing breast cancer of 7% at 80 years and no carriers of the BRCA1 mutation were found<sup>12</sup>. Other series have described BRCA-2 and BRCA-1 gene mutations in 4-16% and 0-4% of male breast cancer cases, respectively<sup>13</sup>. The aforementioned, together with the presence of other specific gene mutations, has led to the recommendation of performing comprehensive genetic counseling in these patients<sup>14</sup>. Unfortunately, genome sequencing tests are not available for the majority of male patients with breast cancer in our

country, mainly due to the high cost of these tests; therefore, risk-based prevention strategies are not accessible.

## HISTOPATHOLOGICAL CHARACTERISTICS

All patients in our study were found to have IDC as their primary histological type, higher than previously described in other series, in which around 84% of patients have IDC<sup>10</sup>. The low incidence of invasive lobular carcinoma could be explained by the infrequent formation of terminal lobes in male breast tissue, a process which is associated to estrogenic exposure.

About 80% of patients in our study expressed either ER or PR by immunohistochemistry and 66.7% of patients expressed both receptors. These numbers are somehow lower than those reported by other authors, in which over 97% of malignant breast tumors in men are positive for ER<sup>13-15</sup>. Although AR expression is common among men with breast cancer<sup>9</sup>, this test could only be performed in two patients, due to economic constraints. Conversely, overexpression of HER2 is very rare in men (8.6% of cases) compared with the 20-30% seen in female patients with breast cancer<sup>16</sup>. In our study, none of the patients overexpressed HER2. Furthermore, the expression of ER/PR and AR has prognostic value among male breast cancer patients, associated with better outcomes in terms of progression-free survival (PFS) and overall survival (OS). Conversely, neither expression of Ki67 or tumor grade has shown to have an impact on prognosis<sup>9</sup>.

Regarding breast cancer subtypes, Luminal B-like/HER-2 negative and Luminal A-like are the most common among male patients with 48.6% and 41.9% of cases, respectively<sup>9,17</sup>. Given that, Ki67 is not routinely performed in our institution due to reimbursement issues, the classification of cases in this study was not possible.

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## TREATMENT

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Although the incidence of BCM has increased significantly in the past 25 years, there is still a lack of prospective data evaluating the optimal management strategy for this group of patients, and thus, the paradigm of treatment for female patients is often followed. However, the vast majority of male patients with breast cancer receive primary surgical treatment with radical mastectomy and only a small percentage of patients is offered a breast-conserving approach since tumors in these population are frequently retroareolar in nature, and thus, conservative surgery is often not possible. Interestingly, retrospective studies show that only 45% of patients treated with a BCS receive adjuvant radiotherapy<sup>9</sup>. In our study, although only two patients were considered as candidates for BCS, both were treated with RT in the adjuvant setting.

Due to the high prevalence of ER/PR-positive tumors among male breast cancer patients, tamoxifen is the drug of choice in the adjuvant and metastatic setting when systemic treatment is warranted. Retrospective evidence has shown the benefit of this drug in OS and PFS when compared to historical controls<sup>18</sup>; however, only 77% of patients with an indication for this treatment actually receive it. Despite the lack of prospective evidence from randomized trials to support its use in male patients, HER2-positive patients are commonly treated with adjuvant trastuzumab given that the potential benefits outweigh the risks. In our study, all patients who were candidates for hormone therapy were treated with tamoxifen either in the adjuvant setting or as the first-line therapy in patients with recurrent or metastatic disease.

To the best of our knowledge, this is the first study that evaluates the clinical and demographic characteristics of BCM in Mexican population. These findings provide information that could help to bet-

ter understand the behavior of this entity. Its retrospective design and the small number of patients included are its principal limitations.

Male breast cancer has become a topic of interest in recent years. This study presents the clinical and pathological characteristics of male patients with breast cancer treated at a referral center in Northeast Mexico. While most of the data presented matches that reported by other authors, some interesting differences unique to our population were observed.

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This investigation was self-funded.

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## CONFLICTS OF INTEREST DISCLOSURE

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The authors declare that there are no conflicts of interest for the publication of this paper.

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## APPROVAL BY THE ETHICS COMMITTEE

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Approval for the study was obtained from the Hospital Universitario "Dr. José Eleuterio González" Ethics Committee.

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## DATA AVAILABILITY

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The data used to support the findings of this study are available from the corresponding author on request.

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